PATENT
Attorney Docket No. ***P06367US03***

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent application of: **MARANAS**, Costas D., et al.

For: METHOD FOR DETERMINING GENE KNOCKOUT STRATEGIES,

the specification of which is being transmitted herewith.

INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Attached are Forms PTO/SB/08A and 08B (formerly Form PTO-1449) listing the relevant art known to the applicant herein. Copies of the listed references are enclosed. The Examiner is requested to consider the references and make them of record.

Applicants submit herewith patents, publications or other information, of which they are aware that they believe may be material to the examination of this application, and in respect of which, there may be a duty to disclose. Legible copies of all items listed in Forms PTO/SB/08A and 08B (formerly Form PTO-1449) accompany this information statement, except those identified above.

The filing of this information disclosure statement shall not be construed as a representation that a search has been made (37 C.F.R. § 1.97(g)), an admission that the

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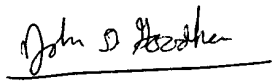
The filing of this information disclosure statement shall not be construed as an admission against interest in any manner. (Notice of January 9, 1992, 1135 O.G. 13-25, at 25.)

Respectfully submitted,



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Attorneys of Record

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 1 of 3

Complete if Known	
Application Number	
Filing Date	
First Named Inventor	MARANAS, Costas D., et al.
Art Unit	
Examiner Name	
Attorney Docket Number	P06367US03

U.S. PATENT DOCUMENTS

Examiner Initials *	Cite No.[1]	Document Number — Number - Kind Code[2] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	1	US- 2002/0168654 A1	11/14/2002	Maranas et al.	
	2	US- 2003/0073092 A1	04/17/2003	Maranas et al.	
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FOREIGN PATENT DOCUMENTS

Examiner Initials *	Cite No.[1]	Foreign Patent Document — Country Code[3] -Number[4]- Kind Code[5] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T[6]

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Sheet 2 of 3

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Application Number	
Filing Date	
First Named Inventor	MARANAS, Costas D., et al.
Group Art Unit	
Examiner Name	
Attorney Docket Number	P06367US03

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No. [1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T [2]
	3	Biebl, H, Menzel, K, Zeng, AP, Deckwer, WD. 1999. "Microbial production of 1,3-propanediol". Appl Environ Microbiol 52: 289-297.	
	4	Burgard, AP, Maranas, CD. 2001. "Probing the performance limits of the Escherichia coli metabolic network subject to gene additions or deletions". Biotechnol Bioeng 74: 364-375.	
	5	Burgard, AP, Maranas, CD. 2003. Optimization-based framework for inferring and testing hypothesized metabolic objective functions. Biotechnol Bioeng 82(6): 670-7.	
	6	Burgard, AP, Vaidyaraman, S, Maranas, CD. 2001. "Minimal Reaction Sets for Escherichia coli Metabolism under Different Growth Requirements and Uptake Environments." Biotechnol Prog 17: 791-797.	
	7	Cameron, DC, Altaras, NE, Hoffman, ML, Shaw, AJ. 1998. "Metabolic engineering of propanediol pathways." Biotechnol Prog 14(1): 116-25.	
	8	Compagno, C, Boschi, F, Ranzi, BM. 1996. "Glycerol production in a triose phosphate isomerase deficient mutant of Saccharomyces cerevisiae". Biotechnol Prog 12(5): 591-5.	
	9	Edwards, JS, Ibarra, RU, Palsson, Bo. 2001. "In silico predictions of Escherichia coli metabolic capabilities are consistent with experimental data". Nat Biotechnol 19(2): 125-30.	
	10	Edwards, JS, Palsson, BO. 2000. "The Escherichia coli MG1655 in silico metabolic genotype: its definition, characteristics, and capabilities". Proc Natl Acad Sci U S A 97(10): 5528-33.	
	11	Gupta, S, Clark, DP. 1989. "Escherichia coli derivatives lacking both alcohol dehydrogenase and phosphotransacetylase grow anaerobically by lactate fermentation." J Bacteriol 171(7): 3650-5.	

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Examiner Initials *	Cite No. [1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T [2]
	12	Hartlep, M, Hussmann, W, Prayitno, N, Meynial-Salles, I, Zeng, AP. 2002. "Study of two-stage processes for the microbial production of 1,3-propanediol from glucose". Appl Microbiol Biotechnol 60(1-2): 60-6.	
	13	Hugler, M, Menendez, C, Schagger, H, Fuchs, G. 2002. "Malonyl-coenzyme A reductase from Chloroflexus aurantiacus, a key enzyme of the 3-hydroxypropionate cycle for autotrophic CO(2) fixation". J Bacteriol 184(9): 2404-10.	
	14	Ibarra, RU, Edwards, JS, Palsson, BO. 2002. "Escherichia coli K-12 undergoes adaptive evolution to achieve in silico predicted optimal growth". Nature 420(6912): 186-9.	
	15	Menendez, C, Bauer, Z, Huber, H, Gad'on, N, Stetter, KO, Fuchs, G. 1999. "Presence of acetyl coenzyme A (CoA) carboxylase and propionyl-CoA carboxylase in autotrophic Crenarchaeota and indication for operation of a 3-hydroxypropionate cycle in autotrophic carbon fixation". J Bacteriol 181(4): 1088-98.	
	16	Segre, D, Vitkup, D, Church, GM. 2002. "Analysis of optimality in natural and perturbed metabolic networks". Proc Natl Acad Sci U S A 99(23): 15112-7.	
	17	Stols, L, Donnelly, MI. 1997. "Production of succinic acid through overexpression of NAD(+)-dependent malic enzyme in an Escherichia coli mutant". Appl Environ Microbiol 63(7): 2695-701.	
	18	Zeikus, JG, Jain, MK, Elankovan, P. 1999. "Biotechnology of succinate acid production and markets for derived industrial products". Appl Microbiol Biotechnol 51: 545-552. Zeng, AP, Biebl, H. 2002. Bulk chemicals from biotechnology: the case of 1,3-propanediol production and the new trends. Adv Biochem Eng Biotechnol 74: 239-59.	
	19	Zhu, MM, Lawman, PD, Cameron, DC. 2002. "Improving 1,3-propanediol production from glycerol in a metabolically engineered Escherichia coli by reducing accumulation of sn-glycerol-3-phosphate". Biotechnol Prog >18(4): 694-9.	

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